TT = Test day treated group value

[0122] 2. LDL and VLDL cholesterol levels were calculated according to the formula:

$$\text{LDL cholesterol in mg/dl} = [\text{ Total cholesterol - HDL cholesterol - } \frac{\text{Triglyceride}}{5}] \text{ mg/dl}$$

VLDL cholesterol in mg/dl = [Total cholesterol - HDL cholesterol - LDL cholesterol] mg/dl.

[0123] **Single dose oral pharmacokinetic studies**

[0124] Male Wistar rats (220 – 250 gm) were used in the experiments. The animals were maintained under standard laboratory conditions and had free access to feed and water *ad libitum*. Before experimentation animals were fasted overnight (~15 h) during which they had free access to water *ad libitum*.

[0125] An amount equivalent to 30 mg of drug was weighed accurately and transferred into a clean mortar and triturated to obtain a fine powder. To this 0.5 ml of 0.25% sodium carboxy methyl cellulose (sodium CMC) was added to obtain a paste. To the obtained paste remaining 2.5 ml of sodium CMC was added to make up the volume to 3 ml. Based on the animal weight appropriate volume (body weight x 3) of the prepared suspension was administered through oral gavage.

[0126] After dosing, at designated time points (0.5, 1, 2, 3, 5, 8, 12 and 24 h) 200 µl of blood was collected from retro orbital plexus into 0.5 ml eppendorff tubes containing EDTA (10 µl of 200 mg/ml solution in Milli Q water). Blood was centrifuged at 12,800 rpm for 5 min and obtained plasma and stored at –20°C till further analysis.

[0127] 100µl plasma was transferred into a clean and dry centrifuge tube. To this internal standard (10 µl of 100 µg/ml) was added and extracted with 2 ml of extraction recovery solvent. The contents were vortexed for 2 min, followed by centrifugation for 10 min at 2800 rpm. Clear organic layer (2 x 0.75 ml) was separated and dried under nitrogen gas at 50°C. The residue was reconstituted with 150 µl of mobile phase and vortexed for 20 sec, from this 50 µl was injected onto HPLC column.

[0128] Pharmacokinetic parameters were calculated by non-compartmental model analysis. The peak plasma concentration (C_{max}) and the corresponding time (T_{max}) were

directly obtained from the raw data. The area under the plasma concentration versus time curve up to the last quantifiable time point, $AUC_{(0-t)}$ was obtained by the linear and log–linear trapezoidal summation. The $AUC_{(0-t)}$ extrapolated to infinity (i.e., $AUC_{(0-\alpha)}$) by adding the quotient of C_{last}/K_{el}, where C_{last} represents the last measurable time concentration and K_{el} represents the apparent terminal rate constant. K_{el} was calculated by the linear regression of the log-transformed concentrations of the drug in the terminal phase. The half-life of the terminal elimination phase was obtained using the relationship $t_{½} = 0.693/ K_{el}$.

Example No.	$AUC_{(0-\infty)}$ (µg.hr/ml)	$AUC_{(0-t)}$ (µg.hr/ml)	C_{max} (µg.hr/ml)	T_{max} (h)	K_{el} (h^{-1})	$T_{½}$(h)
2	319.93 ± 36.19	315.05 ± 34.73	77.23 ± 24.07	0.63 ± 0.25	0.17 ± 0.03	4.25 ± 0.86